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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/062,308	02/01/2002	David L. Rimm	YUA-001.01	2553
25181	7590	04/27/2006	EXAMINER	
FOLEY HOAG, LLP PATENT GROUP, WORLD TRADE CENTER WEST 155 SEAPORT BLVD BOSTON, MA 02110			LIN, JERRY	
			ART UNIT	PAPER NUMBER
			1631	

DATE MAILED: 04/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/062,308

Applicant(s)

RIMM ET AL.

Examiner

Jerry Lin

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 February 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 7-29, 33-40, 42 and 44-46 is/are pending in the application.
- 4a) Of the above claim(s) 33-38 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 7-29, 39, 40, 42, and 44-46 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☐ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: _____.

DETAILED ACTION

Applicants' arguments, filed February 9, 2006, have been fully considered and they are not deemed to be persuasive. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Status of the Claims

Claims 7-29, 39, 40, 42, and 44-46 are under examination.

Claims 33-38 are withdrawn as being drawn to an unelected invention.

Claims 1-6, 30-32, 41, and 43 are cancelled.

Claim Rejections - 35 USC § 112, 1st Paragraph

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 44-46 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Instant claim 44 contains the step of subtracting a percentage of the intensity value for each pixel location in the second image from the intensity value of the same

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pixel location in the first image to obtain an adjusted intensity value, indicative of the biomarker within the subcellular compartment. It is unclear from the claims how one of skill in the art is to determine what percentage of the intensity value in the second image is to be subtracted from the first image. In addition, it is unclear what percentage is needed to create an adjusted intensity value that is indicative of the biomarker within the subcellular compartment. The instant specification contains no teaching of subtracting the percentage of intensity values of the second image from the first image. The specification does not teach what criteria one of skill in the art should use to determine the correct percentage intensity value to subtract from the first image that creates an adjusted intensity value that is indicative of the biomarker within the subcellular compartment. The specification does describe using the percentages of intensity value in page 17, however, the method of using the percentages is not the same as claimed in claim 44. Thus without further guidance and/or method steps one of skill in the art would not be able to make or use the claimed invention.

Claim Rejections - 35 USC § 101

3. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

4. Claims 7-29, 39, 40, 42, 44-46 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The instant claims are drawn to a method of localizing a biomarker in a sub-cellular compartment of the cell that includes obtaining an image of a subcellular

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compartment and an image of a biomarker, finding the intensity values of the first and second images, and comparing the images to determine if the biomarker is within the sub-cellular compartment.

In regards to claims 7-29, 39, 40, 42, 44-46, the instant claims are drawn to a method of processing data (i.e. mathematical algorithm). A mathematical algorithm is non-statutory unless the claims include a step of physical transformation, or if the claims include a useful, tangible and concrete result. It is important to note, that the claims themselves must include a physical transformation step or an useful, tangible and concrete result in order for the claimed invention to be statutory. It is not sufficient that a physical transformation step or a useful, tangible, and concrete result be asserted in the specification for the claims to be statutory. In the instant claims, there is no step of physical transformation, thus the Examiner must determine if the instant claims include a useful, tangible, and concrete result.

In determining if the instant claims are useful, tangible, and concrete, the Examiner must determine each standard individually. For a claim to be "useful," the claim must produce a result that is specific, substantial, and credible. For a claim to be "tangible," the claim must set forth a practical application of the invention that produces a real-world result. For a claim to be "concrete," the process must have a result that can be substantially repeatable or the process must substantially produce the same result again. Furthermore, the claim must recite a useful, tangible, and concrete result in the claim itself, and the claim must be limited only to statutory embodiments. Thus, if

the claim is broader than the statutory embodiments of the claim, the Examiner must reject the claim as non-statutory.

The instant claims do not include any tangible result. A tangible requirement requires that the claim must set forth a practical application of the mathematical algorithm to produce a real-world result. The instant claims are drawn to a method of processing image data. However, the data required may be retrieved from a database and the processing may take place entirely within a computer without any communication with the outside world. Since the instant claims do not rely information to the outside world, the instant claims do not have a real-world result. Thus the instant claims do not include any tangible result.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6. Claims 7, 9-19, 23-29, 39, 40, and 42 are rejected under 35 U.S.C. 102(e)(1) as being anticipated by Harris et al. (US 2003/0036855).

The instant claims are drawn to a method of localizing a biomarker in a sub-cellular compartment of the cell that includes obtaining an image of a subcellular

compartment and an image of a biomarker, finding the intensity values of the first and second images, and comparing the images to determine if the biomarker is within the sub-cellular compartment.

Regarding claims 11, 13, 15, 25, 27, 29, 39, 40, and 42, Harris et al. teach a method that includes using a stain for the first sub-cellular compartment in the first image and a second stain for at least one biomarker (page 22, paragraph 0341-page 23, paragraph 0346); determining the intensity value for the first stain and the second stain and superimposing the images to indicate that the biomarker is within the first sub-cellular compartment (page 16, paragraph 0224- page 17, paragraph 0244; page 22, paragraph 0341-page 23, paragraph 0346; Fig. 24A-26D); a stain is a fluorophore (pages 14-15, paragraph 0188); fixing the cells (page 4, paragraph 0034); using cells that are in tissue (page 5, paragraph 0069; page 14, paragraph 0182).

Regarding claim 7, Harris et al. teach reducing representation of out of focus elements in the image (assigning unqualified pixels a value of 0) (page 16, paragraph 0024- page 17, paragraph 0244).

Regarding claims 9, 12, 16, Harris et al. teach a method wherein the defined area is a nucleus or other organelles (page 22, paragraph 0341-page 23, paragraph 0346; page 21, paragraph 0321).

Regarding claim 10, Harris et al. teach using a biomarker that is a protein (page 22, paragraph 0341-page 23, paragraph 0346; Fig. 24A-26D).

Regarding claims 14, 15 and 17, Harris et al. teach that their method may image the same cell several times at may different wavelengths using three or more different

stains (page 4, paragraph 0035; page 5, paragraph 0069-0070; page 7, paragraphs 0090-0095; page 14, paragraph 0182); and determining the threshold value for each of a plurality of pixels and assigning pixel locations (page 11, paragraph 0145).

Regarding claim 18, Harris et al. teach that the pixel locations in the plurality of pixels in the image of the first stain distribution are the pixel locations in the mask (page 11, paragraph 0143).

Regarding claims 19 and 23, Harris et al. teach wherein the pixels have an intensity value greater than the threshold intensity value (page 16, paragraph 0224-page 17, paragraph 0244).

Regarding claims 24, 26, and 28, Harris et al. teach summing the intensity values to determine total signal intensity (page 15, paragraph 0198).

Response to Arguments

7. The applicants have responded to this rejection by stating that the instant reference does not teach "a novel pixel based method of localizing a biomarker in a cell that is described in independent claim 11." The Examiner disagrees. To paraphrase claim 11, the claim consists of finding the intensity values of the pixels of each image, determining the location of those intensity values/pixels, then comparing those images to see if the pixels of one image is found within certain locations of a second image. Harris et al. determines the intensity values of the pixels of two images (page 22, paragraph 0341-page 23, paragraph 0346). Harris et al. then superimposes the images and finds certain pixels of one image within certain locations of a second image (page

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16, paragraph 0224- page 17, paragraph 0244; page 22, paragraph 0341-page 23, paragraph 0346; Fig. 24A-26D). The instant claims do not manipulate the pixels in any way except by determining the intensity values (which is well known in the art) and locating the pixels (which is well known in the art). Thus Harris et al. teach all the limitations of the instant claim.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Harris et al. (US 2003/0036855) in view of Rigaut et al. (Cytometry (1991) Volume 12, pages 511-524).

The instant claims are drawn to a method of localizing a biomarker in a sub-cellular compartment of the cell that includes obtaining an image of a subcellular compartment and an image of a biomarker, finding the intensity values of the first and second images, and comparing the images to determine if the biomarker is within the sub-cellular compartment, in particular the instant claim is drawn to manipulating an image using images of different depths.

Harris et al. is applied as above.

Harris et al. do not specifically teach manipulating the first images based on the third image.

Rigaut et al. teach a method wherein images are taken at different depths and used to manipulate the image pixel intensities (i.e. features) (page 512, right column).

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the methods of Harris et al. and Rigaut et al. Harris et al. teach a method that utilizes live cell assays for determining the presence of chemical compounds in cells (Harris et al., abstract). Although Harris et al. can determine the presence of chemical compounds in cells, their method does not relate that information to the overall structure of a tissue. Rigaut et al. states that observing the structure of the tissue may be important in studying the location of cellular materials (Rigaut et al., page 511, right column). Rigaut et al. provides a method that preserves the structure of a tissue while still allowing the quantification of nuclear DNA. Thus one of ordinary skill in the art would be motivated to combine the methods of Rigaut et al. with Harris et al. to study the presence of chemical compounds in cells as it relates to tissue.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jerry Lin whose telephone number is (571) 272-2561. The examiner can normally be reached on 10:00am-6:30pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, Ph.D. can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic

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